

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	09/121,798	Confirmation No. 3701
Applicant	:	Robert Bridenbaugh	
Filed	:	July 23, 1998	
Art Unit	:	1636	
Examiner	:	Nancy Treptow Vogel	
Docket No.	:	213-0012US	
Customer No.	:	29855	

EFS Submission
Mail Stop AF
Commissioner for Patents
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Alexandria, VA 22313-1450

PRE-APPEAL BRIEF AND REQUEST FOR REVIEW

Sirs and Mesdames:

Introduction, Request for Extension and Authorization:

Applicants submit this Pre-Appeal Brief for consideration in this application pursuant to the procedure as promulgated on July 12, 2005 in the Official Gazette, and as extended pursuant to the notice of January 10, 2006 in the Official Gazette. This brief is filed concurrently with a Notice of Appeal. A three month extension of time is requested and the extension fee is included herewith by virtue of payment through the EFS portal and the Commissioner is thereby authorized to charge this and any other required fees, or credit any overpayment, to Deposit Account No. 50-1922, referencing Atty Docket No. 213-0012US.

Status of the claims:

Claims 23 – 26 and 28 – 47 are pending in the application. The pending claims are directed to a specific combination of steps for plasmid purification. All pending independent claims include at least a step of filtration through filters of defined chemical composition, glass and nylon, to remove endotoxins. Claim 23 includes at least one passage over a series of filters including a glass fiber and a nylon filter. Claims 33, 37 and 43 and claims dependent therefrom include an additional glass fiber and nylon filtration step. Claims 23 and 33 are reproduced below for convenience and the limitations at issue are highlighted:

23. A method for removing endotoxin from a plasmid DNA solution comprising:
- a) *filtering a solution comprising plasmid DNA through a series of filters including a glass fiber filter and a nylon filter;*
 - b) contacting the solution comprising plasmid DNA with a trimethylamino ethyl (TMAE) anion exchange chromatography resin, the solution having a conductivity at which the plasmid DNA is bound to the resin; washing the resin to elute endotoxin; and eluting the plasmid DNA with a step or continuous gradient of increasing conductivity.
33. A method for removal of endotoxin from a plasmid DNA solution comprising:
- a) *filtering the plasmid DNA solution through a series of filters comprising a glass fiber filter and a nylon filter;*
 - b) loading the filtered plasmid DNA solution onto a column comprising trimethylamino ethyl (TMAE) anion exchange resin, wherein the plasmid DNA solution is loaded onto the column in a loading buffer having a conductivity below which the plasmid DNA would elute from the resin; washing the column with a buffer having a conductivity sufficient to elute endotoxin but not plasmid DNA from the resin; and eluting the plasmid DNA with a step or continuous gradient of increasing conductivity, thereby producing a solution of anion exchange purified plasmid DNA; and
 - c) *filtering the solution of anion exchange purified plasmid DNA through a further series of filters comprising a glass fiber filter and a nylon filter to remove residual endotoxins.*

All claims have been rejected under 35 USC §112, 1st paragraph on the basis that the claimed filters constitute a genus of filters, to wit, any glass or nylon filter having the claimed property of removing endotoxins and that, in the asserted “absence of sufficient recitation of distinguishing identifying characteristics,” the specification does not provide a written description sufficient to show possession of the asserted broad genus.

Clear Error # 1: The Examiner is Clearly Incorrect in Characterizing the Claimed Glass and Nylon Filters as a Genus When they Should be Properly Considered Particular Species of the Broad Genus of Filters

The examiner has clearly erred in characterizing the claimed specific filter types as a genus of filters. It is firmly argued that neither nylon nor glass constitute a genus in the context of the claim but are rather particular chemical constituent species from the broad genus of filters. It is noted that, in contrast with endotoxin removal, for purposes of ultrafiltration a number of different chemical membrane constituents are disclosed in the specification as suitable including “cellulose acetate, polysulfone, polyethersulfone and polyvinylidene difluoride.” See page 13, lines 18 -21 and [0051] of the published application. Other common

filter compositions used in biotechnical applications available at the time of the application, and well known to those of skill in the art, included cellulose nitrates and esters, vinyl chloride-acrylonitrile copolymers, polyethylene and polypropylene, and ceramic membranes. *See* Microfiltration and Ultrafiltration, Principals and Applications, Chapter 15, Biotechnical Applications, Zeman and Zydney, Marcel Dekker, 1996. *(to be submitted upon request)*. It is respectfully but firmly urged that the claimed nylon and glass filters are specific species of the broad genera of filters and that the claimed filters are sufficiently identifiable to one of skill in the art by their stated chemical composition, to wit, glass and nylon.

Clear Error # 2: Even if the Claimed Glass and Nylon Filters are Properly Considered a Genus, the Examiner has Clearly Erred in Finding the Disclosure Insufficient as to Identifying Characteristics of the Genus

The Examiner has asserted that nylon and glass filters are a genus of filters but that Applicants have not supplied sufficient identifying characteristics to evidence possession of the asserted genus. The Examiner fails to read the application as a whole but instead seizes on a single statement on the specification, that “filtration through 0.2 μ m filters, from certain vendors, can be used to remove endotoxin”, to argue that Applicants conceded that only particular filters were suitable. The above quoted passage appears to be the only proffered evidence in support of the Examiner’s burden of presenting a *prima facie* case as to why one of ordinary skill in the art would not find the description sufficient to support the claims. The Examiner’s restrictive reading of a single phrase, likely drafted in the interests of the best mode requirement, to establish failure of possession of the claimed invention is clearly erroneous for several reasons.

First, the Examiners conclusion that only a single porosity is disclosed, 0.2 μ m, is factually incorrect. The specification also specifically teaches use of a porosity of 0.45 μ m or larger: “Pall Ultipor N₆₆ filters and Sartorius Sartopure GF filters have been found to remove substantial endotoxin with high yield of nucleic acid. Preferably, the nucleic acid solution is pre-filtered through a nominal 0.2 μ m or a 0.45 μ m or larger filter before filtration through an absolute 0.2 μ m filter. Glass and nylon filters are preferred.” *See* [0058] of the published application. Further, on page 19, ln. 4 – 6, filtration through a 0.45 μ m filter was taught in a working example. Clearly the porosity of the filters is not the critical feature and to limit the

claims in such way would deny the inventors a scope of protection commensurate with the disclosed advances to the art.

Secondly, in apparent keeping with the best mode requirement, the Applicant disclosed sources of filters that had been found suitable at the time the application was filed according to their tradenames or corporate names. It is noted that the named suitable suppliers of Pall-Filtron, Sartorius and Gelman (page 15, lines 24 – 30) were among the leading filtration suppliers world-wide at the time the application was filed. It is nonetheless appreciated that these names can change over time and would clearly not be permitted in the claims in any event. The Examiner appears to be imposing a requirement of limiting the Applicant to actually tested filters by tradename on the basis of the Applicant's disclosure of best mode sources at the time the application was filed. This restrictive practice is clearly erroneous. The Patent Act and Federal Circuit case law require only a disclosure conveying with reasonable clarity to those of skill in the plasmid purification art that the inventor was in possession of the claimed invention at the time of filing. *See e.g. Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1323 (Fed. Cir. 2000); *Union Oil Co. v. Atlantic Richfield Co.*, 208 F.3d 989, 997 (Fed. Cir. 2000).

A determination of whether one of skill in the art would recognize that an applicant was in possession of a claimed invention at the time of filing includes, inter alia, consideration of: actual reduction to practice; sufficient relevant identifying characteristics; functional characteristics coupled with known or disclosed correlations between function and structure; and level of skill and knowledge in the art. *See e.g. PTO Written Description Training Materials* (Rev. 1, March 25, 2008). In the present case, working example 5 on page 24 of the specification ([0083] – [0085] as published) presents actual reduction to practice of plasmid purification using nylon and glass filters in series to reduce endotoxin.

The Examiner has argued that there is no description of identifying characteristics for recognizing that a particular filter from a particular manufacturer will have the claimed property of removing endotoxins. To the theoretical possibility that there may in fact be some unsuitable glass or nylon filters, such can be readily determined by one of skill in the art standing on the shoulders of the present disclosure. To wit, a plasmid DNA preparation containing a certain level of endotoxin can be run over the test filters and the level determined

afterwards relative to any loss of plasmid DNA. This correlation between structure and function is so straightforward as to not require elaboration. The level of skill and knowledge in the art is high and routine experimentation is often, if not typically, undertaken to identify suitable sources for a particular commodity utilized in the art

Glass and nylon are known chemical constituents that fully define the claimed filter types as select compositional species within the broad genus of filters. The identifying characteristic of the claimed species of glass and nylon is this very chemical makeup. It is noted in this context, that the written description is met for chemicals where the specification literally describes the claimed compounds by structure or name, in the instant case, glass and nylon filters as both disclosed and claimed.

The Applicants surprisingly found that a specific combination of steps for plasmid purification including filtration through filters of the defined chemical compositions of glass and nylon resulted in removal of endotoxins without loss of DNA. The Applicants were in actual possession of this discovery and disclosed the finding with reasonable clarity to those of skill in the art. Satisfaction of the best mode requirement by disclosure of actual filters used should not work to limit the scope of claims to this discovery.

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For the reasons stated herein, it is respectfully submitted that the specification clearly satisfies the written description requirement of 35 USC §112, paragraph 1 as to independent claims 23, 33, 37 and 43, and the claims dependent therefrom. Applicant respectfully requests that the written description rejection be lifted and that the present claims be allowed. Should there be any questions in regard to this submission, please contact Applicant's attorney at 832-446-2421.

Respectfully submitted on **Dec. 22, 2009**,

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